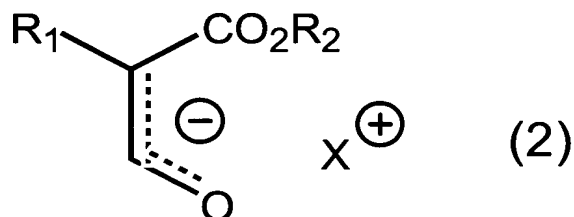


CLAIMS

1. A process for producing a 2-formylacetic ester derivative represented by the general formula (2):



where R_1 represents an alkyl group having 2 to 10 carbon atoms, an optionally substituted aralkyl group having 5 to 15 carbon atoms, or an optionally substituted aryl group having 5 to 15 carbon atoms; R_2 represents an alkyl group having 1 to 10 carbon atoms, or an optionally substituted aralkyl group having 5 to 15 carbon atoms; and X represents H, Li, Na or K, characterized by comprising the steps of:

reacting an acetic ester derivative represented by the general formula (1):



where R_1 and R_2 are the same as described above,

with a base and a formic ester, thereby converting the acetic ester derivative into a 2-formylacetic ester derivative represented by the general formula (2);

and

removing impurities from the reaction mixture into an organic layer formed by addition of an organic solvent and water thereto, while transferring/dissolving the derivative represented by the general formula (2) into a resulting aqueous layer.

2. The process according to claim 1 wherein, in the formulas (1) and (2), R_1 is an alkyl group having 2 to 10 carbon atoms or an optionally substituted aralkyl group having 5 to 15 carbon atoms.

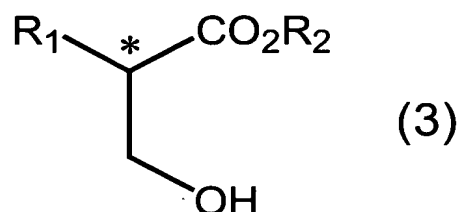
3. The process according to claim 1 or 2 wherein, in the formulas (1) and (2), R_2 is an alkyl group having 1 to 10 carbon atoms.

4. The process according to claims 1, 2, or 3 wherein the base is sodium hydride, sodium metal, or an alkaline metal alkoxide.

5. The process according to claim 1, 2, 3, or 4 wherein the reaction is performed by adding the acetic ester derivative and the formic ester to a solvent containing the base.

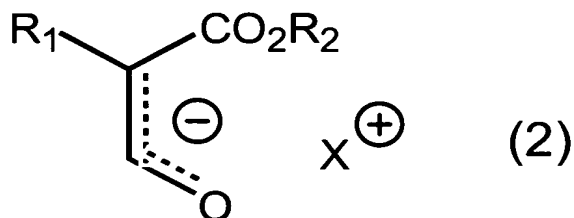
6. The process according to claim 5 wherein the reaction is performed in the solvent containing the base not less than 10% by weight and at a reaction temperature of 20°C or more.

7. A process for producing an optically active 3-hydroxypropionic ester derivative represented by the general formula (3):



where R_1 represents an alkyl group having 2 to 10 carbon atoms, an optionally substituted aralkyl group having 5 to 15 carbon atoms, or an optionally substituted aryl group having 5 to 15 carbon atoms; R_2 represents an alkyl group having 1 to 10 carbon atoms, or an optionally substituted aralkyl group having 5 to 15 carbon atoms; and * represents an asymmetric carbon atom,

characterized by subjecting a 2-formylacetic ester derivative represented by the general formula (2):



where R_1 and R_2 are the same as described above; and X represents H, Li, Na or K,

to the action of an enzymatic source capable of stereoselectively reducing the formyl group thereof,

wherein the R configuration of the derivative represented by the formula (3) is produced by using an enzymatic source which is derived from a microorganism of the genus of Brettanomyces, Cryptococcus, Debaryomyces, Galactomyces, Ogataea, Pichia, Saccharomycopsis, Sporidiobolus, Sporobolomyces, Sterigmatomyces, Torulaspora, Trichosporon, Yamadazyma, Achromobacter, Cellulomonas, Devosia, Hafnia, Jensenia, Klebsiella, Micrococcus, Proteus, Rhodococcus, or Serratia, and capable of R-selectively reducing the formyl group of the derivative represented by the formula (2); or

the S configuration of the derivative represented by the formula (3) is produced by using an enzymatic source which is derived from an microorganism of the genus of Cystofillobasidium, Pichia, Rhodotorula, Torulaspora, Williopsis, Yarrowia, Devosia, Microbacterium, or Micrococcus and capable of S-selectively reducing the formyl group of the derivative represented by the formula (2).

8. The process according to claim 7 wherein in the formulas (2) and (3), R_1 is an alkyl group having 2 to 10 carbon atoms or an optionally substituted aralkyl group having 5 to 15 carbon atoms.

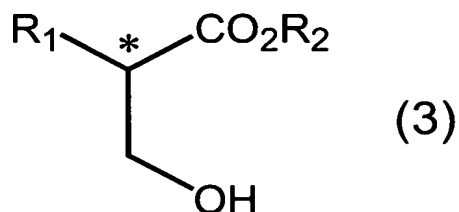
9. The process according to claim 7 or 8 wherein the R configuration of the derivative represented by the formula (3) is produced by using, as the R-selective enzymatic source, an enzymatic source derived from a microorganism selected from the group consisting of Brettanomyces anomalus, Cryptococcus curvatus, Cryptococcus terreus, Debaryomyces nepalensis, Debaryomyces robertsiae, Galactomyces reessii, Ogataea minuta var. minuta, Pichia canadensis, Pichia silvicola, Pichia xylosa, Saccharomycopsis selenospora, Sporidiobolus johnsonii, Sporidiobolus salmonicolor, Sporobolomyces salmonicolor, Sterigmatomyces halophilus, Torulaspora delbrueckii, Trichosporon asteroides, Yamadazyma stipitis, Achromobacter xylosoxidans subsp. denitrificans, Cellulomonas fimi, Cellulomonas sp., Cellulomonas uda, Devosia riboflavina, Hafnia alvei, Jensenia canicruria, Klebsiella planticola, Micrococcus luteus, Proteus inconstans, Rhodococcus erythropolis, Rhodococcus equi, Rhodococcus sp., and Serratia marcescens.

10. The process according to claim 7, 8, or 9 wherein the R-selective enzymatic source is a cultured product of Escherichia coli HB101 (pNTDRG1) (FERM BP-08458), Escherichia coli HB101 (pNTSGG1) (FERM P-18449), Escherichia coli HB101 (pTSBG1) (FERM BP-7119), or Escherichia coli HB101 (pNTRS) (FERM BP-08545); or a processed product thereof.

11. The process according to claim 7 or 8 wherein the S configuration of the derivative represented by the formula (3) is produced by using, as the S-selective enzymatic source, an enzymatic source derived from a microorganism selected from the group consisting of Cystofillobasidium bisporidii, Pichia bispola, Rhodotorula glutinis var. glutinis, Torulaspora globosa, Williopsis saturnus var. mrakii, Williopsis saturnus var. saturnus, Yarrowia lipolytica, Devosia riboflavina, Microbacterium esteraromaticum, and Micrococcus luteus.

12. The process according to claim 7, 8, or 11 wherein the S-selective enzymatic source is a cultured product of Escherichia coli HB101 (pNTDRG1) (FERM BP-08458), or Escherichia coli HB101 (pTSBG1) (FERM BP-7119); or a processed product thereof.

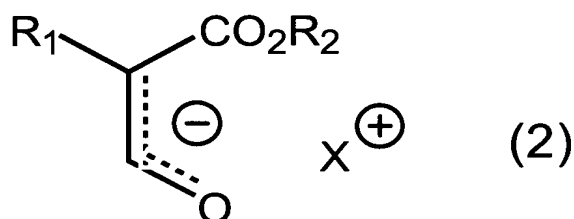
13. A process for producing an optically active 3-hydroxypropionic ester derivative represented by the general formula (3):



where R₁ represents an alkyl group having 2 to 10 carbon atoms, an optionally substituted aralkyl group having 5 to 15 carbon

atoms, or an optionally substituted aryl group having 5 to 15 carbon atoms; R₂ represents an alkyl group having 1 to 10 carbon atoms, or an optionally substituted alkyl group having 5 to 15 carbon atoms; and * represents an asymmetric carbon atom,

characterized by subjecting a 2-formylacetic ester derivative represented by the general formula (2):



where R₁ and R₂ are the same as described above; and X represents H, Li, Na or K,

to the action of an enzymatic source capable of stereoselectively reducing the formyl group thereof,

wherein the R-configuration of the derivative represented by the formula (3) is produced by using an enzymatic source which is derived from a microorganism selected from the group consisting of Candida cantarellii, Candida glabrosa, Candida gropengiesseri, Candida lactis-condensi, Candida magnoriae, Candida maltosa, Candida maris, Candida mogii, Candida pini, Candida rugosa, Candida sorbophila, Candida tropicalis, Candida versatilis, Rhodotorula aurantiaca, Rhodotorula glutinis, Rhodotorula graminis, and Rhodotorula

lactosa and capable of R-selectively reducing the formyl group of the derivative represented by the formula (2); or

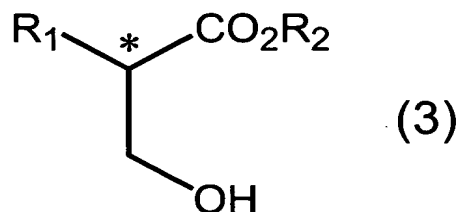
the S-configuration of the derivative represented by the formula (3) is produced by using an enzymatic source which is derived from Candida magnoriae and capable of S-selectively reducing the formyl group of the derivative represented by the formula (2).

14. The process according to claim 13 wherein the R-selective enzymatic source is a cultured product of Escherichia coli HB101 (pNTRCG) (FERM BP-6898) or Escherichia coli HB101 (pNTRGG1) (FERM BP-7858); or a processed product thereof.

15. The process according to claim 13 wherein the S-selective enzymatic source is a cultured product of Escherichia coli HB101 (pNTRCG) (FERM BP-6898) or a processed product thereof.

16. The process according to claim 13 wherein, in the formulas (2) and (3), R_1 is an n-butyl or 3,4-methylenedioxybenzyl group.

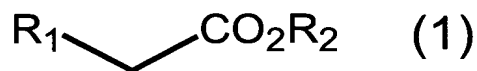
17. A process for producing an optically active 3-hydroxypropionic ester derivative represented by the general formula (3):



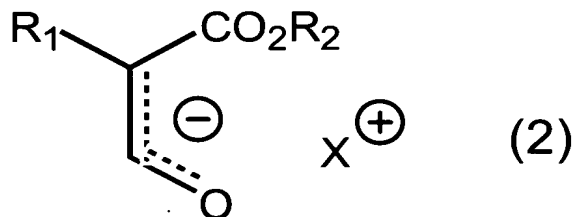
where R_1 represents an alkyl group having 2 to 10 carbon atoms, an optionally substituted aralkyl group having 5 to 15 carbon atoms, or an optionally substituted aryl group having 5 to 15 carbon atoms; and R_2 represents an alkyl group having 1 to 10 carbon atoms, or an optionally substituted aralkyl group having 5 to 15 carbon atoms,; and * represents an asymmetric carbon atom,

characterized by comprising the steps of:

reacting an acetic ester derivative represented by the general formula (1):



where R_1 and R_2 are the same as described above with a base and a formic ester, thereby converting the acetic ester derivative into a 2-formylacetic ester derivative represented by the general formula (2):



where R_1 and R_2 are the same as described above; and X represents H, Li, Na or K;

removing impurities from the reaction mixture into an organic layer formed by addition of an organic solvent and

water thereto, while transferring/dissolving the derivative represented by the general formula (2) into a resulting aqueous layer; and

stereoselectively reducing the derivative represented by the formula (2) by use of an enzymatic source capable of stereoselectively reducing the formyl group of the derivative represented by the formula (2), thereby obtaining the optically active 3-hydroxypropionic ester derivative represented by the general formula (3).

18. The process according to claim 17 wherein, in the formulas (1), (2), and (3), R_1 is an alkyl group having 2 to 10 carbon atoms or an optionally substituted aralkyl group having 5 to 15 carbon atoms.

19. The process according to claim 17 or 18 wherein, in the formulas (1), (2) and (3), R_2 is an alkyl group having 1 to 10 carbon atoms.

20. The process according to claim 17, 18, or 19 wherein the enzymatic source capable of stereoselectively reducing the formyl group of the derivative represented by the formula (2) is derived from a microorganism belonging to the genus Brettanomyces, Candida, Cryptococcus, Debaryomyces, Galactomyces, Ogataea, Pichia, Rhodotorula, Saccharomycopsis, Sporidiobolus, Sporobolomyces, Sterigmatomyces, Torulaspora, Trichosporon, Yamadazyma, Achromobacter, Cellulomonas,

Devosia, Hafnia, Jensenia, Klebsiella, Proteus, Rhodococcus, Serratia, Cystofillobasidium, Williopsis, Yarrowia, Microbacterium, or Micrococcus.

21. The process according to claim 20 wherein the R configuration of the derivative represented by the formula (3) is produced by using an enzymatic source which is derived from a microorganism belonging to the genus of Brettanomyces, Candida, Cryptococcus, Debaryomyces, Galactomyces, Ogataea, Pichia, Rhodotorula, Saccharomycopsis, Sporidiobolus, Sporobolomyces, Sterigmatomyces, Torulaspora, Trichosporon, Yamadazyma, Achromobacter, Cellulomonas, Devosia, Hafnia, Jensenia, Klebsiella, Micrococcus, Proteus, Rhodococcus or Serratia and capable of R-selectively reducing the formyl group of the derivative represented by the formula (2).

22. The process according to claim 21 wherein the enzymatic source capable of R-selective reduction is derived from a microorganism selected from the group consisting of Brettanomyces anomalus, Candida cantarellii, Candida glabrosa, Candida gropengiesseri, Candida lactis-condensi, Candida magnoriae, Candida maltosa, Candida maris, Candida mogii, Candida pini, Candida rugosa, Candida sorbophila, Candida tropicalis, Candida versatilis, Cryptococcus curvatus, Cryptococcus terreus, Debaryomyces nepalensis, Debaryomyces robertsiae, Galactomyces reessii, Ogataea minuta var. minuta, Pichia Canadensis, Pichia silvicola,

Pichia xylosa, Rhodotorula aurantiaca, Rhodotorula glutinis, Rhodotorula graminis, Rhodotorula lactosa, Saccharomycopsis selenospora, Sporidiobolus johnsonii, Sporidiobolus salmonicolor, Sporobolomyces salmonicolor, Sterigmatomyces halophilus, Torulaspora delbrueckii, Trichosporonasteroids, Yamadazyma stipitis, Achromobacter xylosoxidans subsp. denitrificans, Cellulomonas fimi, Cellulomonas sp., Cellulomonas uda, Devosia riboflavina, Hafnia alvei, Jensenia canicruria, Klebsiella planticola, Micrococcus luteus, Proteus inconstans, Rhodococcus erythropolis, Rhodococcus equi, Rhodococcus sp. and Serratia marcescens.

23. The process according to claim 22 wherein the enzymatic source capable of R-selective reduction is a culture product of Escherichia coli HB101 (pNTCRG) (FERMBP-6898), Escherichia coli HB101 (pNTDRG1) (FERM BP-08458), Escherichia coli HB101 (pNTRGG1) (FERM BP-7858), Escherichia coli HB101 (pNTSGG1) (FERM P-18449), Escherichia coli HB101 (pTSBG1) (FERM BP-7119) or Escherichia coli HB101 (pNTRS) (FERM BP-08545); or a processed product thereof.

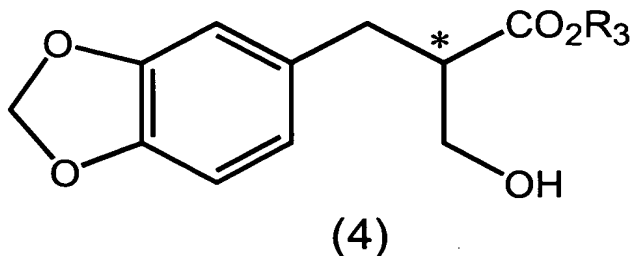
24. The process according to claim 20 wherein the S configuration of the derivative represented by the formula (3) is produced by using an enzymatic source which is derived from a microorganism belonging to the genus of Candida, Cystofillobasidium, Pichia, Rhodotorula, Torulaspora, Williopsis, Yarrowia, Devosia, Microbacterium, or

Micrococcus and capable of S-selectively reducing the formyl group of the derivative represented by the formula (2).

25. The process according to claim 24 wherein the enzymatic source capable of S-selectively reducing the formyl group of the derivative represented by the formula (2) is derived from a microorganism selected from the group consisting of Candida magnoliae, Cystofillobasidium bisporidii, Pichia bispola, Rhodotorula glutinis var. glutinis, Torulaspora globosa, Williopsis saturnus var. mrakii, Williopsis saturnus var. saturnus, Yarrowia lipolytica, Devosia riboflavina, Microbacterium esteraromaticum and Micrococcus luteus.

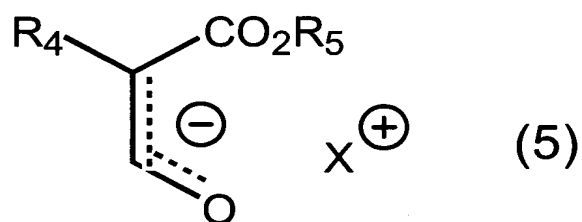
26. The process according to claim 24 or 25 wherein the enzymatic source capable of S-selectively reducing the formyl group of the derivative represented by the formula (2) is a cultured product of Escherichia coli HB101 (pNTCRG) (FERM BP-6898), Escherichia coli HB101 (pNTDRG1) (FERM BP-08458), or Escherichia coli HB101 (pTSBG1) (FERM BP-7119); or a processed product thereof.

27. An optically active
2-(hydroxymethyl)-3-(3,4-methylenedioxyphenyl)-propionic ester derivative represented by the general formula (4):



where R_3 represents an alkyl group having 1 to 10 carbon atoms;
and * represents an asymmetric carbon atom.

28. A 2-formylacetic ester derivative represented by the
general formula (5):



where R_4 represents an alkyl group having 2 to 6 carbon atoms;
 R_5 represents an alkyl group having 1 to 10 carbon atoms; and
 X represents H, Li, Na or K.

29. The 2-formylacetic ester derivative according to claim
28 wherein, in the general formula (5), R_5 is an ethyl group.

30. The 2-formylacetic ester derivative according to claim
28 or 29 wherein, in the general formula (5), R_4 is an ethyl,
propyl, butyl, pentyl or hexyl group.